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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
09/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,971	LE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,15,16,18-20 and 22-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,15,16,18-20 and 22-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 07/05/2007, has been entered.

Claims 1-3 have been amended.

Claims 34-39 have been added.

Claim 21 has been canceled
Claims 8-14 and 17 have been canceled previously.

Claims 1-7, 15-16 and 18-20 and 22-39 are pending and under consideration as they read on the elected invention.

Applicant's election of the species ALS and pain control agent as an additional therapeutic agent in Reply to Election of Species Requirement, filed 10/6/06, has been acknowledged.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 07/05/2007.

The rejections of record can be found in the previous Office Action, mailed 01/03/2007.

3. Priority.

The effective filing date of the instant claims is deemed as follows.

Applicant's assertions concerning priority of the instant application, filed 07/05/2007 (and previously addressed in response to the arguments, filed 10/06/2006), have been fully considered but are not found convincing essentially for the reasons of record.

Again, it appears that the priority of the instant claims may receive a priority date of USSN 08/013,413, filed 02/02/1993, as this appears to be the first USSN in the priority chain for the instant application to disclose the treatment of neurodegenerative diseases, including the elected species ALS.

Again, applicant relies upon treating "chronic inflammatory diseases", wherein neurodegenerative diseases are a subset of inflammatory diseases, wherein the pro-inflammatory cytokine TNF-α is implicated as a significant factor in causing inflammation to support the recitation of the treatment of neurodegenerative diseases, including the elected species ALS, as currently claimed and encompassed by the instant claims.

In contrast to applicant's reliance on the assertion that neurodegenerative diseases are a subset of inflammatory diseases,
the instant claims now recite limitations (e.g., "neurodegenerative", as well as the disclose / elected species such as "ALS") which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the earliest priority applications and did result in filing a continuation-in-part USSN 08/013,413, filed 2/2/93, as this appears to be the first USSN in the priority chain for the instant application to disclose the treatment of neurodegenerative diseases, including the elected species ALS.

Further, neither the priority applications nor the instant application have provided a sufficient description of a representative number of species to represent the entire genus of "neurodegenerative diseases" as well as the specific recitation of neurodegenerative diseases (e.g. ALS), as currently claimed.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Therefore, reliance upon the genus of "TNF-α-related human diseases" and the disclosure of "chronic inflammatory diseases" which may involving the pro-inflammatory cytokine TNF does not provide sufficient written description for "neurodegenerative diseases", including the species such as "ALS" back to the earliest priority USSN 07/670,827, filed 3/18/91, as asserted by applicant's claim for benefit of priority of the instant claims.

Also, with respect to claims 31-33, it is noted that "wherein said anti-TNF chimeric antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4 and/or 5" would appear, at best, to receive a priority date back to USSN 08/192,093, filed 2/4/94 (now U.S. Patent No. 6,284,471).

Also, it is noted that claims drawn to "further comprising administering to the human an effective amount of a pain control agent" "wherein the pain control agent is selected from the group consisting of paracentamol and dextropropoxyphene" recited in claims 15-16 do not receive an earlier priority date, particularly in light of combination therapy with "inhibiting TNFα in a human patient having a neurodegenerative disease", as broadly claimed currently.

While the limited disclosure on pages 57-63 of the instant specification relating to Therapeutic Methods for Treating TNF-Related Pathologies does not appear to support the combination therapies currently claimed in the context of "inhibiting TNFα in a human patient having a neurodegenerative disease", as generically claimed.

Rather, it appears that the claims as filed have drawn from the specific Examples of treating the specific conditions of rheumatoid arthritis to present combination therapies not supported by the specification as filed.

Applicant's apparent reliance on generic disclosure of treating TNF-Related Pathologies with specific therapies associated with particular combination therapy associated with a single or limited species of diseases, namely rheumatoid arthritis, does not provide sufficient direction and guidance to the "combination therapy in the context of "inhibiting TNFα in a human patient having a neurodegenerative disease", as currently claimed.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Therefore, this application repeats a substantial portion of prior USSN 09/756,398, filed 01/08/2001 and adds and claims additional disclosure not presented in the prior application, as indicated above. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

In turn, applicant should amend the first line of the specification to indicate the status of the instant application as a continuation-in-part.

Given the number of continuation-in-part applications, applicant is invited to clarify the support under 35 USC 112, first paragraph, for the priority of the instant claims in the lineage of priority documents for establishing the record for clarity.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

It is noted that entitlement to a filing date does not extend to subject matter, which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

A claim as a whole has only one effective filing date.

See Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

Also, applicant is reminded that a species reads on a genus.

If applicant desires priority prior to 02/02/1993, applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

Applicant's arguments concerning priority have not been found persuasive.

4. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required:
There appears to be insufficient antecedent basis for the written description for the recitation of:
"further comprising administering to the human an effective amount of a pain control agent" "wherein the pain control agent is selected from the group consisting of paracentamol and dextropropoxyphene" recited in claims 15-16 in light of combination therapy with "inhibiting TNFα in a human patient having a neurodegenerative disease", as broadly claimed currently.

Applicant's arguments, filed 07/05/2007, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant directs antecedent basis for the recitation of "paracentamol and dextropropoxyphene" to Tables 5-6 on pages 101-102 of the instant specification for antecedent written support of the instant claims.

However applicant's reliance upon to Tables 5-6 on pages 101-102 of the instant specification is based upon EXAMPLE XX - Clinical Treatment of Rheumatoid Arthritis By a Anti-TNF Antibody or Peptide of the Present Invention.

In contrast to the use of "paracentamol and dextropropoxyphene" clinical treatment of rheumatoid arthritis as supported by the instant specification as-filed;
the instant claims 1, 15 and 16, including the newly submitted claims 35 and 38 are drawn to the treatment of patients with inflammation associated with neurodegenerative disease / amylotrophic lateral sclerosis (ALS)

Therefore, as indicated previously, the only written support for the instant methods accordingly appear to the original filed claims.

Applicant is requested to identify the written support for the instant claims, particularly the recitation of
"further comprising administering to the human an effective amount of a pain control agent" "wherein the pain control agent is selected from the group consisting of paracentamol and dextropropoxyphene" recited in claims 15-16 in light of combination therapy with "inhibiting TNFα in a human patient having a neurodegenerative disease", as broadly claimed currently.

Therefore, applicant is required to amend the instant specification to provide proper antecedent basis for the claimed subject matter.

Alternatively, applicant is requested to identify the written support for the instant claims in the specification as-filed as it reads on treatment of patients with inflammation associated with neurodegenerative disease / amylotrophic lateral sclerosis (ALS)

5. Upon consideration of applicant's amendment, filed 07/05/2007, including the Townsend Statement, filed 10/06/2006, the previous rejection under 35 U.S.C. § 112, first paragraph, enablement concerning the deposit of biological materials, has been withdrawn.

6. Claims 1-7, 15-16, 18-20 and 22-39 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant's arguments in conjunction with various references, filed 07/05/2007, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant submits that the claims are now drawn to methods of inhibiting the action of TNF-α for treating inflammation associated with neurodegenerative diseases in a human.

Further, applicant note that A2-specific antibodies have long half-lives (e.g., REMICADE, infliximab) for in vivo therapeutic uses.

Applicant submits in conjunction with Exhibits
that TNFα antagonists, including TNFα-specific antibodies have been used safely and effectively to treat diseases associated with the pro-inflammatory cytokine TNFα
(e.g., see Exhibit A);
that strategies were known for the delivery of antibodies to the brain, including neurosurgery-based strategies (e.g., see Exhibit B);
that antibodies can cross the blood brain barrier as a therapeutic approach, including consideration in the treatment of Alzheimer disease (e.g., see Exhibits C and D).

With respect to the references employed in the rejection of record,
applicant relies upon the newly submitted recitation of "inflammation associated with".

Further, applicant relies upon the following comments or issues raised in or addressed by the references applied in the rejection of record in order to support of the enablement of the claimed invention in terms of in the context "inflammation associated with neurodegenerative disease".
For example, applicant asserts
that the fact that there is a neuroprotective effect of TNF is not dispositive that there can be no benefit from inhibiting the negative effects of TNF on inflammation in the disease state and
that applicants' disclosure provides ample examples of these benefits to the extent that one of skill in the art would know that inflammation associated with neurodegenerative diseases occurs in connection with the harmful over-production of TNFα, not with the protective effects of low levels of TNF.
that "[i]n the brain, overproduction of TNFα and other pro-inflammatory cytokines has been implicated in a variety of neuropathologies, including the AIDS-demential complex, stroke trauma, multiple sclerosis and Alzheimer's disease" (e.g., see page 179 of Venters et al.).
that while there is controversy regarding normal tissues, Viviani et al. also points out the benefits of a TNFα antibody in damaged tissue,
that while there are conflicting studies regarding the involvement of TNFα in neurotoxic and neuroprotective activities, the use of an antibody to TNFα to treat disease states has been beneficial
such that one of skill in the art would know how to determine when inflammation would be amenable to treatment with anti-TNFα antibodies.

While applicant has provided direction to the possible benefits of administering TNFα anatagonists, including TNFα-specific antibodies to treat inflammation, including "inflammation associated with neurodegeneration"
applicant has not provided sufficient objective evidence to counter the various deficiencies or limitations of treating inflammation in patients with neurodegenerative diseases by targeting TNF-α such as the conflicting results of the role of TNF-α in neurodegeneration, the formidable challenges of treating such inflammation / neuroinflammation, in general as well as in targeting TNF-α, in particular as indicated by the references employed in the rejection of record and provided herein.

In addressing New Therapeutic Strategies and Drug Candidates for Neurodegenerative Diseases (Ann. N.Y. Acad. Sci. 1035: 290-315, 2004) (see entire document) Greig et al. notes the following after acknowledging the validity of anti-TNF antibodies, including the instant A2/-cA2-specific antibodies in treating autoimmune / inflammatory disease.

These medications, however, are large macromolecules that minimally traverse administration and have negligible brain penetration – thereby precluding their utility in neurodegenerative disorders.

See entire document, particularly page 304, paragraph 1.

Hays (Current Pharmaceutical Design 4: 335-348, 1998) (see entire document) reviews Therapeutic Approaches to the Treatment of Neuroinflammatory Diseases notes that:

Studies involving interference with TNF-α and its role in neurodegeneration have produced conflicting results, including that given multiple biological activities of certain TNF-α inhibitors, it is difficult to determine that the protective effects were a result of the TNF-α mechanism.

See pages 339-340, Tumor Necrosis Factor-α.

Further, in describing the formidable challenge for halting the progression of neurodegeneration, Hays also notes there are many problems with producing effective drugs, given the plethora of molecular mechanisms in neuroinflammation and the lack of appropriate animal models.

See page 345, Conclusion of Hays.

In reviewing Cytokines Role in Neurodegenerative Events, Viviani et al. (Toxicology Letters 149: 85-89, 2004) (see entire document) notes the controversy associated with the neurotoxic properties of the cytokine TNF-α, including the lack of causing neuronal death in healthy brain / neuronal tissues as well as indications of neuroprotective effects of TNF-α. Here, the various parameters contributing to the circumstances combinatorial effects allowing a single cytokine to transmit diverse signals.

See Contribution of Cytokines of Neurodegeneration and Neurotoxicity, particularly page 86, column 2, paragraph 1.

Similar observations of contrary findings concerning the neurotoxic / neuroprotective properties of TNF-α are acknowledged by Venters et al. (TINS 23: 175-180, 2000) (see entire document), including that :

The exact factors responsible for shifting the roles of TNF-α from neurotoxicity to neuroprotection are not known.

See TNF-α as a Death Signal on pages 175-176, particularly page 176, columns 1-2, overlapping paragraph.

Given the relative incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims, a rejection under 35 USC 112, first paragraph for lack of enablement was appropriate
See MPEP 2164.08

Also, see Enzo Biochem Inc. v. Calgene Inc. 52 USPQ2d 1129 (CAFC 1999), which stands for making the determination of enablement by looking back to the filing date of patent application and determining whether undue experimentation would have been required to make and use claimed invention at that time and since factors if applied from proper temporal perspective and useful methodology for determining enablement.

"A recurring problem is whether a specification that sets forth a single or a limited number of examples can be enabling of broad claims when the subject matter concerns biological materials or reactions which are generally considered to be unpredictable."
See Enzo Biochem Inc. v. Calgene Inc. 52 USPQ2d 1129, 1138 (CAFC 1999).

There is insufficient direction and guidance as to how choose which "neurodegenerative diseases" are amenable to treatment with anti-TNF-α antibodies. The claims do not appear to take in account the broad diversity of diseases encompassed and targeted by the claimed invention (e.g. see Claims and page 57 of the instant specification), nor the variability of the neurotoxic and neuroprotective effects of TNF-α in such neurodegenerative diseases or during the course of a particular neurodegenerative disease.

Given the breadth of "neurodegenerative diseases", the absence of working examples and the formidable challenge of treating neurodegenerative diseases with TNF-α-specific inhibitors, including the treating neurodegenerative diseases with the claimed TNF-α-specific antibodies,
there appears to be insufficient guidance and direction as to how to how to practice the breadth of treating "neurodegenerative diseases" to be treated by administering "a TNF-α-inhibiting amount of an TNF-α antibody" to treat inflammation associated with "any neurodegenerative disease".

The specification does not teach how to extrapolate data obtained from in vitro and in vivo inhibition of certain immune or inflammatory responses with anti-TNF-α antibodies to the development of effective in vivo human therapeutic methods to treat viral infections, commensurate in scope with the claimed invention. Therefore, reliance upon the anti-inflammatory properties of anti-TNF-α antibodies does not provide for the skilled artisan to predict that treatment of viral infections or the scope of viral infections encompassed by the claimed methods would be predictable.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 18 24 (CCPA 1970).

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective neurodegenerative therapies with anti-TNF-α antagonist / antibody-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting neurodegenerative diseases, broadly encompassed by the claimed invention.

Again, applicant is invited to provide objective evidence to support either the bread of "neurodegenerative diseases" targeted by the claimed invention, including the elected invention drawn to "ALS", and to amend the claims to recite those neurodegenerative diseases accordingly.

Applicant's arguments have not been found persuasive.

7. Again, it is noted that treating "ALS" as the elected neurodegenerative species appears to be free of the prior art.

As addressed above, treating "ALS" and the breadth of "neurodegenerative diseases" is subject to the enablement rejection under 35 USC 112, first paragraph, above.

The prior art has been extended to the treatment of "multiple sclerosis" as a species that reads on treating "neurodegenerative diseases". Also, see Neurodegenerative Diseases on page 58 of the instant specification for the instant disclosure of "multiple sclerosis".

8. Applicant's assertions concerning priority of the instant application, filed 07/05/2007 (and previously addressed in response to the arguments, filed 10/06/2006), have been fully considered but are not found convincing essentially for the reasons of record.

Again, it appears that the priority of the instant claims may receive a priority date of USSN 08/013,413, filed 02/02/1993, as this appears to be the first USSN in the priority chain for the instant application to disclose the treatment of neurodegenerative diseases, including the elected species ALS.

Therefore, applicant's arguments, filed 07/05/2007, which relies upon the priority of the instant claims to 03/19/1991, have been fully considered but have not been found convincing for the reasons of record and as addressed above in Section 3 on Priority.

The following of record is reiterated for applicant's convenience.

Claims 1-7, 15-16, 18-20 and 22-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Le et al. (WO 92/16553) in view of Beck et al. (Acta Neurol. Scand. 78 : 318-323,1988), Chofflon et al. (Eur. Cytokine Netw. 3 : 523-531, 1992) and Selmaj et al. (Ann Neurol 30 : 694-700, 1991) and in further evidence in providing pain management as basic to management of treating neurologic disorders, as evidenced by The Merck Manual Of Diagnosis And Therapy, Sixteenth Edition, 1992 (edited by Berkow et al., Merck Research Laboratories, Merck & Co., Rahway, NJ, 1992; see pages 1407-1409) at the time the invention was made.

Le et al. teach the generation of recombinant cA2-specific anti-TNF-α antibodies, fragments and derivatives (e.g. see pages 9-11; page 13, paragraph 1 and Examples on pages 45- 74) of the instant invention (see entire document, including Description of the Prior art, Summary of the Invention, Detailed Description of the Preferred Embodiments and Claims)., which are useful for treating subject having a pathology or condition associated with levels of substance reactive with an anti-TNF antibody, in particular for those subjects having excess levels of TNF , including targeting chronic immune or autoimmune pathologies (e.g. see page 34, paragraph 1)

Le et al. differs from the claimed invention by not disclosing multiple sclerosis, including that role of TNF in multiple sclerosis, including the demyelination associated with TNF.

Beck et al. teach that TNF triggers exacerbation of clinical events in multiple sclerosis patients and this cytokine plays a role in maintaining disease in chronic progressive and invalidating forms (See entire document, including Abstract). Beck et al. also teaches that experimental mice with cerebral manifestations can be protected with anti- TNF-α antibodies (e.g. see pages 322-323, overlapping paragraph).

Chofflon et al. (Eur. Cytokine Netw. 3 : 523-531, 1992) expands the finding of Beck et al. (e.g. see paragraph 1 of the Discussion on page 528) in that the clinical relapse in multiple sclerosis patients was associated with increased TNF-α (see entire document, including Abstract and Discussion). Also, Chofflon et al. teach that immunosuppressive drugs on cytokine secretion could make in possible that earlier treatment would reduce the extent of tissue lesions, slow down the evolution of the disease and attenuate the disability (e.g. see page 529, column 1, paragraph 5 – column 6, paragraph 1).

Selmaj et al. teach the use of anti-TNF antibodies to inhibit effectively the development of EAE, an inflammatory demyelinating disease of the CNS that is used as a model of human demyelinating disease multiple sclerosis (see Introduction on page 694 concerning the EAE model) (see entire document, including Abstract). Selmaj et al. conclude that anti-TNF therapy appeared to operate at a step subsequent to the generation of autoimmune cells, which may be particularly relevant to the development of new therapeutic strategies for diseases like multiple sclerosis which can alleviate lesion progression (see page 699, column 1, paragraph 1).

With respect to the claimed recitation of "wherein the pain control agent is selected from the group consisting of paracentamol and dextropropoxyphene" and

given that pain management was basic to management of treating neurologic disorders, as evidenced by The Merck Manual Of Diagnosis And Therapy, Sixteenth Edition, 1992 (edited by Berkow et al., Merck Research Laboratories, Merck & Co., Rahway, NJ, 1992; see pages 1407-1409),

it was obvious that one of ordinary skill in the would have motivated to provide pain control, including the use of known paracentamol and dextropropoxyphene, in the management of various neurologic or neurodegenerative disorders/diseases as standard practices at the time the invention was made. It was obvious to use and/or substitute equivalents known for the same purpose, includintg the selection of known materials based upon it suitability or its intended use, which was pain control in the management of various disorders/diseases.

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to include targeting the inflammatory / autoimmune disorder of multiple sclerosis with anti-TNF-α antibodies in order to diminish the deleterious effects of TNF-α in this disease, including the expectation of success of inhibiting demyelination, given the role of TNF-α in demyelination and the ability to neutralize the deleterious effects of TNF-α with anti- TNF-α antibodies, including the instant A2 / cA2 / infliximab anti TNF-α antibody specificity of the claimed invention. The claimed dosages and modes of administration including local and parental administration for the particular disease was obvious to the ordinary artisan at the time the invention was made in meeting the needs of the patient and the nature of the condition being treated as routine practice (also see pages 34-36 of Le et al.) From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Again, as noted above and in the previous Office Action, mailed 01/03/2007, applicant's assertions based upon priority of the instant claims have not been found persuasive.

Applicant's arguments have not been found persuasive.

9. Claims 1-7, 15-16, 18-20 and 22-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,991,791 essentially for the reasons of record.

Although the recitation of the instant and patented claims differ, all of the instant and patented claims are drawn to the same or nearly the same cA2-specific TNF-α-specific antibodies having the same or nearly the same functional properties of neutralizing TNF-α-mediated activities in the treatment of neurodegenerative diseases. The patented claims anticipate or render obvious the instant methods of treating neurodegenerative diseases with anti-TNF-α antibodies. The differences in the recitation of dosages and modes of administration between the instant and pending claims were well known and practiced at the time the invention was made by the ordinary artisan to meet the needs of the patient and the nature of the targeted disease.

Applicant will address this matter in regard to the pending claims upon indication of allowable claims.

10. Claims 1-7, 15-16, 18-20 and 22-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4, 5, 7-10, 12, 14, 21, 23-24, 30, 35, 37 and 52-89 of copending USSN 10/227,488.

Although the recitation of the instant and patented claims differ, all of the instant and patented claims are drawn to the same or nearly the same A2-specific TNF-α-specific antibodies having the same or nearly the same functional properties of neutralizing TNF-α-mediated activities in the treatment of neurodegenerative diseases. The patented claims anticipate or render obvious the instant methods of treating neurodegenerative diseases with anti-TNF-α antibodies. The differences in the recitation of dosages and modes of administration between the instant and pending claims were well known and practiced at the time the invention was made by the ordinary artisan to meet the needs of the patient and the nature of the targeted disease.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant will address this matter in regard to the pending claims upon indication of allowable claims.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, Ph.D., J.D.
Primary Examiner
Technology Center 1600
September 12, 2007